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=> d his

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L2             1 S 3416-24-8/RN
L3             1 S 3616-42-0/RN

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L12          605 S L7 (L) PREP/RL
L13           32 S L9 (L) PREP/RL
L14          134 S L5 (L) (L11 OR L12)
L15           17 S L5 (L) L11 (L) L12
L16          122 S L14 AND PD<19970114
L17            0 S L16 AND FERMENT?
L18            3 S L14 (L) FERMENT?
L19          190 S FERMENT? (L) (L7 OR L9)
L20            3 S L19 (L) L5
L21          122 S L16
L22            7 S L21 AND INHIBIT? AND PRODUCT
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=> d' ibib ab 1-3

L20 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:634531 HCAPLUS
DOCUMENT NUMBER: 136:258038
TITLE: Analysis of the chromosome sequence of the legume symbiont Sinorhizobium meliloti strain 1021
AUTHOR(S): Capela, Delphine; Barloy-Hubler, Frederique; Gouzy, Jerome; Bothe, Gordana; Ampe, Frederic; Batut, Jacques; Boistard, Pierre; Becker, Anke; Boutry, Marc; Cadieu, Edouard; Dreano, Stephane; Gloux, Stephanie; Godrie, Therese; Goffeau, Andre; Kahn, Daniel; Kiss, Erno; Lelaure, Valerie; Masuy, David; Pohl, Thomas; Portetelle, Daniel; Puhler, Alfred; Purnelle, Benedicte; Ramsperger, Ulf; Renard, Clotilde; Thebault, Patricia; Vandenbol, Micheline; Weidner, Stefan; Galibert, Francis
CORPORATE SOURCE: Laboratoire de Biologie Moleculaire des Relations Plantes-Microorganismes, Unite Mixte de Recherche (UMR) 215 Centre National de la Recherche Scientifique (CNRS), Institut National de la Recherche Agronomique, Chemin, Tolosan, F-31326, Fr.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(17), 9877-9882
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sinorhizobium meliloti is an .alpha.-proteobacterium that forms agronomically important N2-fixing root nodules in legumes. We report here the complete sequence of the largest constituent of its genome, a 62.7% GC-rich 3654,135-bp circular chromosome. Annotation allowed assignment of a function to 59% of the 3341 predicted protein-coding ORFs, the rest exhibiting partial, weak, or no similarity with any known sequence. Unexpectedly, the level of reiteration within this replicon is low, with only two genes duplicated with more than 90% nucleotide sequence identity, transposon elements accounting for 2.2% of the sequence, and a few hundred short repeated palindromic motifs (RIME1, RIME2, and C) widespread over the chromosome. Three regions with a significantly lower GC content are most likely of external origin. Detailed annotation revealed that this replicon contains all housekeeping genes except two essential genes that are located on pSymB. Amino acid/peptide transport and degrdn. and sugar metab. appear as two major features of the S. meliloti chromosome. The presence in this replicon of a large no. of nucleotide cyclases with a peculiar structure, as well as of genes homologous to virulence determinants of animal and plant pathogens, opens perspectives in the study of this bacterium both as a free-living soil microorganism and as a plant symbiont.
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:68590 HCAPLUS
DOCUMENT NUMBER: 132:121532
TITLE: Glucosamine fermentation with recombinant microorganisms with mutations in the glucosamine-6-phosphate metabolic pathway
INVENTOR(S): Berry, Alan; Burlingame, Richard P.; Millis, James R.
PATENT ASSIGNEE(S): DCV, Inc. D/B/A Bio-Technical Resources, USA
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000004182	A1	20000127	WO 1999-US15976	19990715	
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6372457	B1	20020416	US 1998-115475	19980715	
AU 9951028	A1	20000207	AU 1999-51028	19990715	
EP 1095158	A1	20010502	EP 1999-935577	19990715	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002520067	T2	20020709	JP 2000-560279	19990715	

PRIORITY APPLN. INFO.:	US 1998-115475	A	19980715
	US 1997-35494P	P	19970114
	WO 1998-US800	A2	19980114
	WO 1999-US15976	W	19990715

AB The present invention relates to a method and materials for producing **glucosamine** by **fermn.** of a genetically modified microorganism. Included in the present invention are genetically modified microorganisms useful in the present method for producing **glucosamine**, as well as recombinant nucleic acid mols. and the proteins produced by such recombinant nucleic acid mols. Thus, a modified Escherichia coli strain with the nagA-D genes deleted, the manXYZ genes mutationally inactivated, and the glmS gene replaced with an inducible mutant glmS gene encoding a **glucosamine-6-phosphate synthase** resistant to **glucosamine-6-phosphate** inhibition was constructed. In **fermentor** cultures, **glucosamine** concns. in excess of 12 g/L were obtained with this E. coli strain.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1998:493700 HCAPLUS
DOCUMENT NUMBER:	129:121714
TITLE:	Process for production of N-glucosamine
INVENTOR(S):	Berry, Alan; Burlingame, Richard P.; Millis, James R.
PATENT ASSIGNEE(S):	Bio-Technical Resources, USA; Berry, Alan; Burlingame, Richard P.; Millis, James R.
SOURCE:	PCT Int. Appl., 91 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3

PATENT INFORMATION:

WO 9830713	A1	19980716	WO 1998-US800	19980114	
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9859604	A1	19980803	AU 1998-59604	19980114	
US 6372457	B1	20020416	US 1998-115475	19980715	

PRIORITY APPLN. INFO.:	US 1997-35494P	P	19970114
	WO 1998-US800	W	19980114

AB The present invention relates to a method for producing glucosamine by

fermn. of a genetically modified microorganism.

=> d ibib ab 1-7

L22 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:392564 HCAPLUS
DOCUMENT NUMBER: 127:47021
TITLE: Substrate binding is required for assembly of the active conformation of the catalytic site in Ntn amidotransferases: evidence from the 1.8 .ANG. crystal structure of the glutaminase domain of **glucosamine 6-phosphate synthase**. [Erratum to document cited in CA125:136326]
AUTHOR(S): Isupov, Michail N.; Obmolova, Galya; Butterworth, Susanna; Badet-Denisot, Maria-Ange; Badet, Bernard; Polikarpov, Igor; Littlechild, Jennifer A.; Teplyakov, Alexei
CORPORATE SOURCE: Dep. Chem. Biological Scis., Univ. Exeter, Exeter, EX4 4QD, UK
SOURCE: Structure (London) (**1997**), 5(5), 723
CODEN: STRUE6; ISSN: 0969-2126
PUBLISHER: Current Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The catalytic mechanism described for **glucosamine 6-phosphate synthase** was based on the mechanism of penicillin hydrolysis by penicillin acylase proposed by Duggleby et al. (1995) to which ref. should have been made: Duggleby, H.J., Tolley, S.P., Hill, C.P., Dodson, E.J., Dodson, G. and Moody, P.C.E. (1995) Nature 373, 264-268.

L22 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:460296 HCAPLUS
DOCUMENT NUMBER: 125:136326
TITLE: Substrate binding is required for assembly of the active conformation of the catalytic site in Ntn amidotransferases: evidence from the 1.8 .ANG. crystal structure of the glutaminase domain of **glucosamine 6-phosphate synthase**
AUTHOR(S): Isupov, Michail N.; Obmolova, Gayla; Butterworth, Susanna; Badet-Denisot, Marie-Ange; Badet, Bernard; Polikarpov, Igor; Littlechild, Jennifer A.; Teplyakov, Alexei
CORPORATE SOURCE: Dep. Chem. Biological Scis., Univ. Exeter, Exeter, EX4 4QD, UK
SOURCE: Structure (London) (**1996**), 4(7), 801-810
CODEN: STRUE6; ISSN: 0969-2126
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Amidotransferases use the amide nitrogen of glutamine in a no. of important biosynthetic reactions. They are composed of a glutaminase domain, which catalyzes the hydrolysis of glutamine to glutamate and ammonia, and a synthetase domain, catalyzing amination of the substrate. To gain insight into the mechanism of nitrogen transfer, we examd. the structure of the glutaminase domain of **glucosamine 6-phosphate synthase** (GLMS). The crystal structures of the enzyme complexed with glutamate and with a competitive **inhibitor**, Glu-hydroxamate, have been detd. to 1.8 .ANG. resoln. The protein fold has structural homol. to other members of the superfamily of N-terminal nucleophile (Ntn) hydrolases, being a sandwich of antiparallel .beta. sheets surrounded by two layers of .alpha. helixes. The structural homol. between the glutaminase domain of GLMS and that of phosphoribosyl pyrophosphate (PRPP) amidotransferase (the only other Ntn amidotransferase whose structure is known) indicates that they may have diverged from a common ancestor. Cys1 is the catalytic nucleophile in GLMS, and the nucleophilic character of its thiol group appears to be increased through general base activation by its own .alpha.-amino group.

Cys1 can adopt two conformations, one active and one inactive; glutamine binding locks the residue in a predetd. conformation. We propose that when a nitrogen acceptor is present Cys1 is kept in the active conformation, explaining the phenomenon of substrate-induced activation of the enzyme, and that Arg26 is central in this coupling.

L22 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:1295 HCAPLUS
DOCUMENT NUMBER: 120:1295
TITLE: Glucose regulation of transforming growth factor-.alpha. expression is mediated by **products** of the hexosamine biosynthesis pathway
AUTHOR(S): Daniels, Marc C.; Kansal, Preeti; Smith, Tom M.; Paterson, Andrew J.; Kudlow, Jeffrey E.; McClain, Donald A.
CORPORATE SOURCE: Veterans Adm. Med. Cent., Birmingham, AL, 35294, USA
SOURCE: Mol. Endocrinol. (**1993**), 7(8), 1041-8
CODEN: MOENEN; ISSN: 0888-8809
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have recently shown that glucose and **glucosamine** regulate the transcription of transforming growth factor-.alpha. (TGF.alpha.) in rat aortic smooth muscle (RASM) cells. Based on the increased potency of **glucosamine** compared to glucose, the authors hypothesized that stimulation of TGF.alpha. transcription by glucose is mediated through the hexosamine biosynthesis pathway. The yeast cDNA for the rate-limiting enzyme of this pathway, **glutamine :fructose-6-phosphate amidotransferase** (GFA), was therefore expressed in RASM cells. GFA-transfected cells showed an increase in GFA activity, exhibiting a 2.2-fold increase in the synthesis of **glucosamine-6-phosphate**, the first **product** of the hexosamine biosynthetic pathway. To test the effect of GFA overexpression on TGF.alpha. transcriptional activity, cells were transiently cotransfected with GFA along with a reporter plasmid contg. the firefly luciferase gene under control of the TGF.alpha. promoter. GFA-transfected cells exhibited a glucose-dependent 2-fold increase in TGF.alpha. activity compared to control cells. Maximal stimulation of TGF.alpha. luciferase activity by **glucosamine**, however, was equiv. in GFA- and control-transfected cells, confirming that the stimulation obsd. by both agents operated through the same pathway. This increase in TGF.alpha. activity was **inhibited** (85% at 0.5 mM glucose and 69% at 30 mM glucose) by the glutamine analog and **inhibitor** of GFA, 6-diazo-5-oxonorleucine (10 .mu.M). Control studies confirmed that the increased TGF.alpha.-luciferase activity in the GFA-expressing cells was not an artifact of altered growth, survival, or transfection efficiency. Expts. using pharmacol. agents to stimulate or **inhibit** protein kinase C and cAMP-dependent kinase do not support a role for these second messengers in the signaling pathway. Tunicamycin **inhibited** the ability of glucose to stimulate TGF.alpha. activity, suggesting that protein glycosylation does play a role. The authors conclude that **products** of the hexosamine biosynthesis pathway mediate the stimulation by glucose of TGF.alpha. in aortic smooth muscle cells.

L22 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:119586 HCAPLUS
DOCUMENT NUMBER: 118:119586
TITLE: Investigation of the **inhibition** pathway of **glucosamine synthase** by N3-(4-methoxyfumaroyl)-L-2,3-diaminopropanoic acid by semiempirical quantum mechanical and molecular mechanics methods
AUTHOR(S): Tarnowska, M.; Oldziej, S.; Liwo, A.; Grzonka, Z.; Borowski, E.
CORPORATE SOURCE: Dep. Chem., Univ. Gdansk, Gdansk, PL-80-952, Pol.
SOURCE: Eur. Biophys. J. (**1992**), 21(4), 273-80

CODEN: EBJOE8; ISSN: 0175-7571
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Glucosamine 6-phosphate synthase** (EC 2.6.1.16) is a promising target in antifungal drug design. It has been reported that its potent **inhibitor**, N3-(4-methoxyfumaroyl)-L-2,3-diaminopropanoic acid (FMDP), inactivates the enzyme by the Michael addn. of the SH group to the FMDP mol. followed by cyclization reactions. Here, using semiempirical MNDO, PM3, and mol. mechanics methods, the energetics and kinetic possibility of the formation of various stereoisomers of the **products** of cyclization of the Michael addn. **products** detected exptl. were investigated. It was found that the substituted 1,4-thiazin-3-one can be formed in 1 step under alk. conditions; the stereoisomers of this compd., predicted to be the most stable on the basis of theor. calcns., were also the dominant ones in reality.

L22 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:194297 HCAPLUS
DOCUMENT NUMBER: 112:194297
TITLE: **Glucosamine-6-phosphate synthase** from Escherichia coli: determination of the mechanism of inactivation by N3-fumaroyl-L-2,3-diaminopropionic derivatives
AUTHOR(S): Kucharczyk, Nathalie; Denisot, Marie Ange; Le Goffic, Francois; Badet, Bernard
CORPORATE SOURCE: Lab. Bioorg. Biotechnol., ENSCP, Paris, 75231, Fr.
SOURCE: Biochemistry (**1990**), 29(15), 3668-76
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A mechanistic investigation of the inactivation of E. coli **glucosamine-6-phosphate synthase** by N3-(4-methoxyfumaroyl)-L-2,3-diaminopropionate (FMDP) was undertaken. On the basis of the known participation of the N-terminal cysteine residue in this process, model reactions between FMDP and L-cysteine and between FMDP and the synthetic decapeptide, Cys-Gly-Ile-val-Gly-Ala-Ile-Ala-Gln-Arg, corresponding to the N-terminal protein sequence, were studied. The results allowed a pathway to be proposed that was in perfect agreement with the biochem. results: enzyme inactivation arose from Michael addn. of glutamine-binding site cysteine-1 on the fumaroyl double bond at the .beta.-position of the ester group. Upon denaturation under slightly alk. conditions, this adduct underwent cyclization to a transient succinimide adduct, which rearranged into the stable 2-substituted 1,4-thiazin-3-one-5-carboxylate involving participation of the cysteine amino group. The tryptic radiolabeled peptides purified from [3H]FMDP-treated enzyme and resistant to Edman degrdn. coeluted with the **products** resulting from the model reaction between the synthetic decapeptide and the **inhibitor**.

L22 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:146073 HCAPLUS
DOCUMENT NUMBER: 108:146073
TITLE: **Glucosamine synthetase** from Escherichia coli: kinetic mechanism and **inhibition** by N3-fumaroyl-L-2,3-diaminopropionic derivatives
AUTHOR(S): Badet, Bernard; Vermoote, Patricia; Le Goffic, Francois
CORPORATE SOURCE: Lab. Bioorg. Biotechnol., ENSCP, Paris, 75231, Fr.
SOURCE: Biochemistry (**1988**), 27(7), 2282-7
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB N3-(4-Methoxyfumaroyl)-L-2,3-diaminopropionic acid (FMDP), a member of a new class of glutamine analogs, was investigated as an **inhibitor** of pure E. coli glucosamine phosphate synthetase (I). **Product**

and dead-end **inhibition** studies indicated an ordered assocn. to the enzyme with the sugar mol. binding prior to substrate or **inhibitor**. The inactivation exhibited pseudo-1st-order kinetics, was irreversible, and occurred faster in the presence of fructose 6-phosphate, a behavior previously reported for the partially purified enzyme from Salmonella typhimurium. FMDP was found to be one of the most efficient **inhibitors** of I to date. The **inhibition** occurred with partial covalent incorporation of L-FMDP into I. In the presence of fructose 6-phosphate, enzyme inactivation with [2-3H]-DL-FMDP was assocd. with the incorporation of 0.75 equiv of **inhibitor** and with the modification of 0.78 SH residue per enzyme subunit. This result is the 1st evidence for covalent entrapment of the entire **inhibitor** mol. following FMDP-mediated I inactivation. Preliminary inactivation with 6-diazo-5-oxo-L-norleucine, known to alkylate selectively the N-terminal cysteine residue, completely prevented radioactivity incorporation. Therefore, this **inhibitor** is postulated to covalently modify I through direct addn. of the thiol nucleophile from the terminal cysteine residue to the Michaelis acceptor, so acting as an affinity label rather than a mechanism-based **inhibitor**.

L22 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:204266 HCAPLUS
DOCUMENT NUMBER: 102:204266
TITLE: Synthesis of 3,4-iminocyclohexyl-glycine and its N-benzyloxycarbonyl derivative
AUTHOR(S): Dzieduszycka, Maria; Martelli, Sante; Borowski, Edward
CORPORATE SOURCE: Dep. Pharm. Technol. Biochem., Tech. Univ. Gdansk, Gdansk, Pol.
SOURCE: Int. J. Pept. Protein Res. (**1985**), 25(1), 99-104
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 102:204266
AB The title compds. I [R = H, PhCH2O2C (Z)] were prepd. from prepd. from cyclohexenylglycines II (R1 = Z, CF3CO) via an addn. reaction with iodine isocyanate (III). Thus, III was added to II (R1 = Z) to give addn. **products** IV (R2 = Z, R3 = NCO) as a mixt. of the 2 possible 3- and 4-positional isomers. The latter were treated with MeOH to give the corresponding IV (R2 = Z, R3 = NHCO2Me) (as 2 isomers), which were cyclized in the presence of KOH to give I (R = Z). II (R1 = CF3CO) was converted to I (R = H) via IV (R2 = CF3CO, R3 = NHCO2Me). I (R = H) **inhibited glucosamine synthetase**.